REMARKS

The present application is submitted in reply to the final office action dated September 1, 2011 ("Office Action").

Claim 1 is drawn to a method of reducing radiation-induced normal tissue damage. To more distinctly point out and more particularly define the subject matter of the claimed invention, Applicant has added an identifying step. This identifying step is inherently required by the method of previously amended claim 1. Indeed, a method of reducing radiation-induced normal tissue damage, of course, is intended to be applied to a subject that has been or is at risk of being exposed to radiation.

The amendment should be entered as it raises no new issues that will require further consideration or search and also does not touch the merits of the application within the meaning of 37 C.F.R. § 1.116(b). More specifically, claim 1 has been amended to explicitly recite a step of identifying a subject has been or is at risk of being exposed to radiation, which is an inherent step of claim 1.

Claims 1, 3, 7-16, and 24-31 are pending. Among them, claims 1, 11, 14-16, and 29 are under examination; and claims 3, 7-10, 12, 13, 24-28, 30, and 31, covering non-elected species, have been withdrawn.

Applicant respectfully requests that the Examiner reconsider this application in view of the following remarks.

Rejection under 35 U.S.C. § 112 (Written Description)

The Examiner rejects claims 1, 24, and 30 for failing to comply with the written description requirement on the ground that new matter has been introduced into the rejected claims that cover reducing radiation-induced normal tissue damage in a *cancer-free* subject. See the Office Action, page 2, last paragraph through page 4, second paragraph; emphasis added. Applicant respectfully traverses and will discuss claim 1 first.

Claim 1 is drawn to a method of reducing radiation-induced normal tissue damage. As pointed out above, it has been amended to recite a step of identifying a subject that has been or is at risk of being exposed to radiation, a step inherently required

by the method. Note that claim 1 is limited to a subject that has been or is at risk of being exposed to radiation, but not to a subject having cancer or being at risk of having cancer.

The Examiner asserts that "the invention as a whole contemplated the treatment of cancer, as is evidenced through the specification." See the Office action, page 3, second paragraph, last sentence. Applicant disagrees.

As stated in the Specification, "the present invention relates to the treatment of radiation …-induced injuries." See page 1, lines 8 and 9.

A person skilled in the art, in view of this statement, would have understood that the method of increasing therapeutic gain in caner radiotherapy is merely a particular embodiment of the claimed invention, i.e., a method of radiation-induced injuries. As discussed below, other embodiments, such as a method of reducing radiation-induced normal tissue damage in a cancer-free subject, are also included in the method of claim 1.

Indeed, it is well known in the art that a subject can be exposed to radiation in many different situations, such as (1) under cancer radiotherapy and (2) during nuclear plant accidents (e.g., at Chernobyl and Fukushima nuclear plants). In situation (1), the subject is a cancer patient. However, in situation (2), the subject has a greater than 99% chance of being *cancer-free*.[1] In other words, the subject treated by the method of claim 1 can be *cancer-free*. Indeed, as shown in the Specification, in the radiation experiments described in Examples 3-8, 10, and 13, *no cancer cells* were introduced into adult female Sprague Dawley rats, which were used as an animal model. See page 22, lines 16-19.

In view of the above remarks, Applicant submits that, contrary to the Examiner's assertion, the Specification as a whole does not teach treating or preventing cancer; rather, it teaches reducing radiation-induced normal tissue damage in a radiation-exposed subject, which may or may not have cancer or be at risk of having cancer. Indeed, the Specification fully supports claim 1 directed to a method of reducing radiation-induced

[1] It is well known in the art that less than 1% of the world population has cancer. See, e.g., www.cdc.gov/Features/CancerStatistics/ attached hereto as "Exhibit A."

normal tissue damage in a subject that may or may not have cancer or be at risk of having cancer.

In sum, the Examiner errs in stating that new matter has been introduced into claim 1 for covering a method of reducing radiation-induced normal tissue damage in a *cancer-free* subject.

Applicant now turns to the two rejected claims, i.e., claims 24 and 30, which have been withdrawn but are considered and rejected by the Examiner on the same "new matter" ground.

Claim 24 is drawn to a method of reducing radiation-induced normal tissue damage in a *cancer-free* subject, a particular embodiment of claim 1. For at least the same reasons set forth above, claim 24 also does not include new matter.

Claim 30, dependent from claim 24, is limited to a non-elected histone hyperacetylating agent species. As this claim, like claim 24, covers reduction of radiation-induced normal tissue damage in a *cancer-free* subject, it also does not include new matter for the same reasons set forth above.

Rejection under 35 U.S.C. § 102

The Examiner rejects claims 1, 11, 14-16, and 29 for lack of novelty over Samid, US Patent 5,877,213 ("Samid"). See the Office Action, page 4, penultimate paragraph. Applicant respectfully traverses.

Again, claim 1 will be discussed first.

According to the Examiner, Samid teaches a method of treating and preventing cancer with phenylacetic acid and its derivatives, e.g., phenylbutyrate, in combination with radiotherapy. Although this reference does not teach or suggest using phenylbutyrate to reduce radiation-induced normal tissue damage, which is covered by claim 1, the Examiner contends that it inherently teaches such a use on the ground that the population of subjects treated by the Samid method is the **same** as that targeted by the method of claim 1. See the Office Action, page 5, second paragraph. Applicant respectfully disagrees for reasons set forth in the following three paragraphs.

To promote clarity, Applicant has amended claim 1 to explicitly recite a step inherently required by claim 1, i.e., a step of identifying a subject that has been or is at risk of being exposed to radiation. This amendment to claim 1 has made clear that the population of subjects targeted by the method of claim 1 is one that has been or is at risk of being exposed to radiation. As pointed out above, the just-mentioned population includes the subjects that may be cancer-free or not be at risk of having cancer. See page 7, last paragraph, *supra*. Thus, contrary to the Examiner's assertion, this population is NOT the **same** as the population targeted by the Samid method, which only includes subjects suffering from cancer or at risk of having cancer. As such, Samid does not anticipate claim 1, even though there is overlap between the population targeted by the method of claim 1 and that targeted by the Samid method.

Applicants would like to bring to the Examiner's attention that a skilled artisan would have understood the difference between the identifying step inherently required by the Samid method (i.e., identifying a subject suffering from cancer or at risk of having cancer) and the identifying step recited in amended claim 1 (i.e., identifying a subject that has been or is at risk of being exposed to radiation). In other words, the Samid method and the method of claim 1 use two different approaches to identify their different targets.

Needless to say, two different approaches that identify the same target are not the same. It is simply wrong to assert that they are the same on the ground that they identifying the same target. Here, as pointed out above, the target of claim 1 may be cancer-free or not be at risk of having cancer. For even stronger reasons, the Samid identifying step and that of claim 1 are different, as their targets are not necessarily the same. Given the two different identifying steps, the method disclosed in Samid is different from the method of claim 1.

In view of the above remarks, Applicant respectfully submits that claim 1 is not anticipated by Samid.

Nor are claims 11 and 14-16, and 29, all of which depend from claim 1.

Note that the Examiner has considered claim 29, even though it depends from withdrawn claim 24. In any event, Applicant would like to point out that claim 24,

dependent from claim 1, is also novel over Samid for at least the same reasons set forth above.

Withdrawn Claims

In the restriction requirement dated December 19, 2006, the Examiner required election of four species and two subspecies. In response, Applicant elected radiotherapy as a treatment species, proliferating malignant disease as a subject species, sodium phenylbutyrate as a histone hyperacetylating agent species, and mouth wash as a pharmaceutical carrier species. Further, Applicant elected ionizing radiation as a treatment subspecies and head and neck cancer as a subject subspecies.

In the Office Action, the Examiner has considered claims 1, 11, 14-16, and 29, which read on these elected species, and withdrawn claims 3, 7-10, 12, 13, 24-28, 30 and 31, which read on the non-elected species. See the Office Action, page 2, lines 11-13.

Applicant would like to bring to the Examiner's attention a rule set forth in 37 CFR § 1.141, which is reproduced below:

> Two or more independent and distinct inventions may not be claimed in one national application, except that **more than one species of an invention** [] may be specifically claimed in different claims in one national application, provided the application also includes an **allowable claim generic to all the claimed species and all the claims to species in excess of one are written in dependent form** [] (emphases added).

Clearly, this rule requires that the Examiner also consider non-elected species claims, after a generic claim has been held to be allowable.

Turning to this application, **claim** 1, citing the general terms "histone hyperacetylating agent," "subject," and "pharmaceutical carrier," is **generic to all the species** recited in dependent claims 3, 7-10, 12, 13, 24-28, 30, and 31. As discussed above, claim 1, a generic claim, is allowable. Pursuant to the above-quoted rule, the Examiner should also consider the non-elected histone hyperacetylating agent species, the non-elected subject species (i.e., cancer-free subject), and the non-elected

pharmaceutical carrier species recited in claims 3, 7-10, 12, 13, 24-28, 30, and 31, all of which **depend from generic claim 1**.

Applicant submits that, for at least the reasons that claim 1 is allowable, the withdrawn claims dependent therefrom, including claims 3, 7-10, 12, 13, 24-28, 30, and 31, are also allowable. It is therefore requested that the Examiner allow these claims.

CONCLUSION

It is believed that all of the pending claims have been addressed. However, the absence of a reply to a specific rejection, issue or comment does not signify agreement with or concession of that rejection, issue or comment.

In addition, because the arguments made above may not be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed.

Finally, nothing in this paper should be construed as an intent to concede any issue with regard to any claim, except as specifically stated in this paper, and the amendment of any claim does not necessarily signify concession of unpatentability of the claim prior to its amendment.

No fee is believed to be due. Please apply any other charges or credits to Deposit Account No. 50-4189, referencing Attorney Docket No. 55701-004002.

Respectfully submitted,

Date: 12-1-11

Y. Rocky Tsao

Y. Rocky Tsao, Ph.D., J.D.
Attorney at Law
Reg. No. 34,053

Customer No. 69713
Occhiuti Rohlicek & Tsao LLP
10 Fawcett Street
Cambridge, MA 02138
Telephone: (617) 500-2503
Facsimile: (617) 500-2499